REMARKS

Claims 1-4 and 8-27 are all the claims pending in the application.

The above amendments insert the words for the acronym MDON and do not represent new matter. Support for this amendment can be found at page 1 in the last sentence of paragraph 1 and the first sentence of paragraph 2.1.

1. 112 Rejection – Indefiniteness

Claims 2, 8, 17, 19 and 20 have been rejected under 35 U.S.C. § 112 for being indefinite for using the acronym "MDON." This rejection is deemed moot in view of the above amendments to those claims. Withdrawal of this rejection is respectfully requested.

2. 112 Enablement Rejection

Claims 1-4 and 8-27 have been rejected under 35 U.S.C. § 112 for allegedly being non-enabling for not reasonably providing enablement for a method of making a localized mutation in any target gene in a plant cell. This rejection is respectfully traversed.

The Examiner has acknowledged that the present application enables making localized mutations in the ALS and GFP genes but has not taught a method of making localized mutation in other genes *in situ* in a plant cell. The Applicants respectfully point out that identifying the mutation that results in a desired trait is itself not part of the present claims. The present claims are directed to methods of making localized mutations – mutations to genes that are known (the mutation is known) in the art and that have been sequenced at least in the region where the mutation is desired. All of the present claims require the **recombinogenic oligonucleobase** to contain regions that are both homologous and heterologous to the native gene being mutated. The prior amendment to Claims 1 and 16 requires that the mutations cause a desired trait. Thus,

the mutation must be known in order to conduct the presently claimed process. For example, Section 4.6 in the specification spanning pages 11 and 12 identifies several mutated genes and their encoded mutated proteins that cause a desired trait. This represents a starting point for the presently claimed processes.

Regarding the Examiner's other reasons for supporting this enablement rejection and in particular the applicability of the teachings of the Kmiec patents, the Applicants point to Section 4.2 of the Specification where they teach how to handle the location and type of mutation introduced by a MDON. The Applicants also point again to the Walker Declaration already of record as evidence that the present claims are enabled.

In view of the above, it is respecfully requested that the present 112 enablement rejection is not justified and withdrawal of the same is respectfully requested.

3. 102 Rejection – Svab, et al., (1990)

Claims 1 and 16 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Svab, et al 1990. This rejection is respectfully traversed.

Svab, et al., does not disclose a method for making a localized mutation in a target gene. Svab, et al. disclose the TRANSFORMATION of a plant chloroplast with a mutated gene. This chloroplast transformation involves a mechanism that includes the insertion of foreign genetic sequence potentially by homologous replacement which would be expected since chloroplast DNA has evolved from prokaryotic organisms. Svab, et al., employed a 9.6 kb plasmid that contained the mutated gene on a 3.7 kb Sac 1-EcoRV fragment. Rather than making a localized mutation in a native plant gene, Svab, et al. transform a plant cell with a mutated gene and

cannot be considered an anticipation of the present claims. In view of the above, withdrawal of the 102 rejection is respectfully requested.

103 Rejection

Claims 1-4 and 8-27 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Kmiec '181 in view of Applicants admissions. This rejection is respectfully traversed.

The Examiner's argument for obviousness is basically that (1) Kmiec taught the use of recombinogenic oligonucleobases to produce localized mutations but **not** with the gene gun or biolistics methods, (2) Dunder et al. teach **TRANSFORMATION** of plant cells and (3) the Applicant has admitted that the genes and the transformation of specific crops listed in the Specification (p. 8-9 and 12-20) were known in the art. The Applicants agree with the above three points individually but disagree that they form the basis of a valid obviousness rejection under 35 U.S.C. § 103. While the Kmiec recombinagenic nucleobase technology was indeed known it employs small single stranded molecules with short regions of secondary structure making it fragile. The short regions of secondary structure, however, are **critical** to its function. Both the small size and the secondary structure effect of the integrity of the whole recombinagenic nucleobase molecule. Biolistics transformation technology, on the other hand, involved large pieces of DNA that contained whole genes and regulatory sequences, typically in plasmids of several thousands of paired nucleotides containing both coding and regulatory sequence regions. The biolistics transformation technology employed harsh chemical (salts) and physical (shear) conditions in delivering the DNA into the plant cell—conditions whose effects on recombinogenic oligonucleobases was **unknown** at the time the present invention was made.

Because of all the above-described differences between the prior art and the presently claimed methods it is impossible to justify an obviousness rejection based on the art of record. First, there is no teaching to combine the Kmiec recombinagenic nucleobase mutation technology with the biolistics transformation technology of Dunder, et al. Second, there is no evidence of a likelihood of success of the combination of prior art references in view of the differences and uncertainties readily apparent between the recombinagenic nucleobase mutation technology and the biolistics transformation technologies. Taking all of these differences into account would make the skilled artisan doubtful that the presently claimed methods would actually succeed in working. See Beetham and Metz Declarations which are incorporated herein by reference.

For all of the above reasons, the present 103 rejection cannot be maintained. Withdrawal of this rejection is respectfully solicited.

Conclusion

In view of the above, reconsideration and allowance of Claims 1-4 and 8-27 in this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,

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Washington, D.C. 20231

Date: June 3, 2002

Signed: _____
Elaine E. Calimquim

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

2. The method of claim 1, wherein the recombinagenic oligonucleobase is a [MDON] mixed duplex oligonucleotide (MDON) and each of the homologous regions contains an RNA segment of at least 6 RNA-type nucleotides.

8. The method of claim 2, wherein the adhering step is performed in a solution comprising 1.1-1.4 M NaCl and 18-22 μM spermidine and at least 14 μg/ml [MDON] mixed duplex oligonucleotide (MDON).

17. The method of claim 16, wherein the recombinagenic oligonucleobase is a [MDON] mixed duplex oligonucleotide (MDON) and each of the homologous regions contains an RNA segment of at least 6 RNA-Type nucleotides.

19. The method of claim 17, wherein the sequence of the target gene between the first and the second fragments differs from the sequence of the intervening region of the [MDON] mixed duplex oligonucleotide (MDON) at a mismatched nucleotide and the mutation of the target gene is located adjacent to the mismatched nucleotide.

20. The method of claim 17, wherein the sequence of the target gene between the first and the second fragments differs from the sequence of the mutator segment of the [MDON] mixed duplex oligonucleotide (MDON) at a mismatched nucleotide and the mutation of the target gene is located at the mismatched nucleotide.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,

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Signed: Elaine S. Calimquim